

CLAIMS

1. Use, for the implantation or insertion of a solid (1, 9) or semi-solid (18) formulation, intended to be placed in a precise depot site (T) of a body, containing at least one active principle, the said formulation being of solid or semi-solid consistency such that it is able to persist for a certain period in the site, and containing a limited dose of active principle for a treatment in a targeted zone of the body, of a device comprising a part placed inside the body of the patient with means of packaging of the solid or semi-solid form, means of positioning allowing these means of packaging to be led to the site of deposition, means of injection or of insertion at this depot site, and means of withdrawal after injection or insertion, and a part left outside with means of operation of the functions of the device.

2. Use according to Claim 1, characterized in that the said means of packaging of the solid or semi-solid form are placed from the outset at the end of the device intended to be led to the site of deposition.

3. Use according to one of Claims 1 and 2, characterized in that the said means of packaging are arranged to allow the solid or semi-solid formulation to have a thin and elongated, especially cylindrical, form.

4. Use according to Claim 3, in which the said form of the formulation is approximately cylindrical, characterized in that the diameter of the means of packaging is such that the form of the formulation has a diameter of between 0.1 and 2 to 3 millimetres.

5. Use according to Claim 4, characterized in that the said means of packaging are arranged to allow the solid or semi-solid formulation to have a minimum length/diameter ratio of 10.

6. Use according to one of Claims 1 to 5, characterized in that the means of packaging of the solid or

semi-solid forms are also the means of positioning and of injection.

7. Use according to one of Claims 3 to 6, characterized in that the said device comprises a piston (14) inside a needle (13) which can be operated in a trocar (9) and/or a catheter (12).

8. Use according to one of Claims 3 to 6, characterized in that the means of conditioning, positioning and injection comprises a needle (13).

9. Use according to Claim 8, characterized in that the said needle (13), once operated, can be orientated with respect to the device by elastic preshaping or preconstraint or by mechanical means.

10. Use according to Claim 8, characterized in that the external means of operation of the device allow, in a sequential fashion, the injection of the needle (13), the advancement of the piston (14) as far as the bevel (13b) of the needle, to deposit the solid or semi-solid form, the withdrawal of the needle around the piston (14) and the combined withdrawal of the needle and of the piston.

11. Use according to Claim 10, characterized in that the sequential operations of the device starting from external means are controlled remotely and in order with the aid of two movable stops of which the first (10) is arranged on a push button (20) coaxial to the piston (14), and the second (15) is a tubular piece inserted between the guide (12) and the push button (20).

12. Formulation intended to be placed in a precise site of deposition in a body, containing at least one active principle, the said formulation being of solid or semi-solid consistency such that it is able to persist for a certain period in the site, and containing a limited dose of active principle for a treatment in a targeted zone of the body, and having a form making it capable of being placed by a device according to one of Claims 1 to 11.

13. Formulation according to Claim 12, characterized in that it is a delayed-release formulation.

14. Formulation according to one of Claims 12 and 13, characterized in that it contains a low dose of active principle with respect to the customary dose, for a treatment by the systemic route, of the active principle considered.

15. Formulation according to one of Claims 12 to 14, characterized in that it has a thin and elongated, especially cylindrical, form.

16. Formulation according to Claim 15, characterized in that it has a diameter of between 0.1 and 2 to 3 mm.

17. Formulation according to one of Claims 15 and 16, characterized in that the form has a minimum length/diameter ratio of 10.

18. Formulation according to one of Claims 12 to 17, of solid nature, capable of being deformed by being prestrained in a device according to one of Claims 1 to 11 to regain its shape in situ.

19. Formulation according to one of Claims 12 to 18, characterized in that it is arranged in order that the release of the active principle takes place in an anatomical cavity into which it has been introduced.

20. Formulation according to Claim 19, characterized in that it has a form designed to be able to be imprisoned in an anatomical cavity of the body while avoiding the displacement or the elimination of the formulation.

21. Formulation according to Claim 20, characterized in that it is prestrained in the said means of packaging and regains a non-rectilinear shape once placed in its depot site.

22. Formulation according to Claim 20, in which the length and the diameter of the formulation are arranged to avoid its elimination or its displacement.

23. Formulation according to one of Claims 12 to 22, characterized in that the said formulation and the active principle which it contains are arranged in

order that the release of the active principle takes place in the secretions of a mucous membrane.

24. Formulation according to one of Claims 19 to 23, in which the said cavity or mucous membrane is a cavity or mucous membrane of the facial or ORL sphere.

25. Formulation according to Claim 23, in which the said mucous membrane is a tracheopulmonary mucous membrane.

26. Formulation according to Claim 23, in which the said mucous membrane is the buco-oesophageal mucous membrane.

27. Formulation according to one of Claims 23 to 26, in which the said formulation is arranged in order to be placed on the surface of the said mucous membrane such that the active principle is transported by the mucus.

28. Formulation according to one of Claims 23 to 26, in which the said formulation is arranged to be placed inside the mucous membrane.

29. Formulation according to Claim 28, characterized in that the said formulation and the active principle which it contains are arranged for injection into the sub-palpebral mucous membrane.

30. Formulation according to one of Claims 19 to 29, characterized in that it comprises a corticoid suited to the treatment, in a cavity, cavity wall or mucous membrane, of naso-sinusoid polyposis, of allergic or non-allergic rhinitis, of types of non-infectious otitis or sinusitis, by introduction into the maxillary, phenoidal or frontal sinus, the nasal mucous membrane, the ethmoidal cells or the cavum tympani.

31. Formulation according to one of Claims 12 to 18, characterized in that the said formulation and the active principle which it contains are arranged for introduction into or around the vascular wall by intra- or transluminal injection.

32. Formulation according to Claim 31, which can be used especially after transluminal percutaneous

angioplasty, comprising an active principle for the prevention or the treatment of restenosis.

33. Formulation according to Claim 32, containing angiopeptin on its own or combined with another active principle, especially heparin.

34. Formulation according to one of Claims 12 to 18, characterized in that the said formulation and the active principle which it contains are arranged to be introduced into or under a tumour tissue for an antitumour action.

35. Formulation according to Claim 34, in which the active principle comprises a photosensitive product.

36. Formulation according to one of Claims 12 to 18, characterized in that the said formulation and the active principle which it contains are arranged for an intra- or peri-articular injection.

37. Formulation according to one of Claims 12 to 37, characterized in that it contains an anti-inflammatory active principle.

38. Formulation according to one of Claims 12 to 36, characterized in that it contains a high concentration of active principle of between 20 and 100%.

39. Formulation according to Claim 38, characterized by a concentration of active principle of between 40 and 100%.

40. Formulation according to Claim 39, characterized by a concentration of active principle of between 50 and 100%.

41. Delayed-release formulation according to one of Claims 12 to 40, characterized in that the active principle is combined with a polylactide-glycolide (PLGA) copolymer excipient.

42. Solid formulation according to Claim 41, produced in implant form.

43. Formulation according to one of Claims 12 to 42, characterized in that it contains an active principle of peptide or protein nature.

44. Solid delayed-release formulation, intended to be placed in a body, containing at least one active

principle and a biodegradable excipient, characterized in that the excipient is a polylactide-glycolide (PLGA) copolymer, and in that the concentration of active principle is between 40 and 100%.

5 45. Delayed-release formulation according to Claim 44, characterized in that the concentration of active principle is between 50 and 100%.

46. Delayed-release formulation according to one of Claims 44 and 45, characterized in that it has a thin and elongated form with a diameter not exceeding 3 mm.

10 47. Delayed-release formulation according to Claim 46, characterized by a diameter not exceeding 2 mm.

48. Delayed-release formulation according to Claim 46, characterized by a diameter of the order of 0.1 mm.

49. Delayed-release formulation according to one of Claims 44 to 48, characterized by a minimum length/diameter ratio of 10.

20 50. Delayed-release formulation according to one of Claims 44 to 49, characterized in that it contains an active principle of peptide or protein nature.

51. Assembly for the implantation and insertion of a solid (1, 9) or semi-solid (18) formulation containing an active principle, according to one of Claims 12 to 50, in a precise depot site of the body, characterized in that it comprises a device defined in any one of Claims 1 to 11 and, in the said device, a formulation (1, 9, 18) to be delivered, contained in

25

30 the said means of packaging.

52. Assembly according to Claim 51, characterized in that it is arranged to be inserted inside a trocar.

53. Assembly according to Claim 51, characterized in that it is arranged to be inserted inside a catheter.

35 54. Assembly according to Claim 51, characterized in that it is arranged to be inserted inside an endoscope.

55. Assembly according to Claim 51, characterized in that it is arranged to be inserted inside a instrument adapted for a surgical route of approach.

56. Use of an active principle for the production of a formulation according to any one of Claims 12 to 50.

57. Solid delayed-release formulation for parenteral administration comprising a homogeneous mixture of an active principle in the non-dispersed state forming a continuous phase of which at least one part is in direct contact with the exchange surface of the formulation and of the exterior biological medium, and of a biodegradable biocompatible excipient, in which the quantity of active principle is at least 50% by weight with respect to the total weight of the formulation, and having a release profile which is independent of the composition of the excipient, of the molecular weight of the excipient or of the active principle/
excipient weight ratio, the release profile being essentially exclusively dependent on the total quantity of active principle present in the formulation.

58. Delayed-release formulation according to Claim 57, characterized in that the biodegradable biocompatible excipient is a polymer or copolymer of lactic and/or glycolic acid or a mixture of polymers and/or copolymers of lactic and/or glycolic acid.

59. Delayed-release formulation according to Claim 58, characterized in that the said biodegradable biocompatible polymer is a copolymer of lactic acid and glycolic acid (PLGA).

60. Delayed-release formulation according to any one of Claims 57 to 59, characterized in that the said biodegradable biocompatible polymer is a copolymer of lactic and glycolic acid having an intrinsic viscosity in chloroform at .1 g per 100 ml of greater than 0.6 dl/g.

61. Delayed-release formulation according to Claim 59 or Claim 60, characterized in that the

copolymer of lactic acid and glycolic acid is of hydrophilic nature.

62. Delayed-release formulation according to one of Claims 57 to 60, characterized in that, when it is placed *in vitro* in a physiological liquid medium, it liberates almost the whole of the active principle in less than a week, and, when it is placed *in vivo* subcutaneously or intramuscularly, has a release of active principle over a period substantially greater than one week.

63. Delayed-release formulation according to one of Claims 57 to 62, characterized in that it comprises a mixture of the active principle and the excipient which is homogeneous at all points.

64. Delayed-release formulation according to any one of Claims 57 to 63, characterized in that the release takes place in a single diffusion phase of the active principle.

65. Delayed-release formulation according to any one of Claims 57 to 64, characterized in that the active principle represents at least 51%, advantageously at least 60%, preferably at least 70% and up to 99.999% by weight with respect to the total weight of the formulation, the excipient representing less than 50%, preferably less than 49%, and more advantageously less than 30% by weight with respect to the total weight of the formulation.

66. Delayed-release formulation according to any one of Claims 57 to 65, characterized in that the active principle is a peptide, a peptide analogue or a protein, especially LHRH or an analogue of LHRH, especially Triptoreline.

67. Delayed-release formulation according to any one of Claims 57 to 66, characterized in that it is in cylindrical form and has a diameter less than or equal to 3 mm, preferably less than 1 mm.

68. Delayed-release formulation according to any one of Claims 57 to 67 for injection by the intramuscular or subcutaneous route.

69. Delayed-release formulation according to any one of Claims 57 to 68, characterized in that it is in the form of an implant.

5 70. Use of a delayed-release formulation according to any one of Claims 57 to 69 for the preparation of a medicament intended for a parenteral injection in dry form.

10 71. Process for preparation of a delayed-release formulation according to any one of Claims 57 to 69, comprising the steps consisting in:

- producing a homogeneous mixture of the active principle and the excipient, containing at least 50% of active principle;

- compacting the said mixture; and
- 15 - extruding the said compacted mixture in the molten state.

72. Process for preparation of a formulation according to any one of Claims 12 to 50 and 57 to 69, comprising the steps consisting in:

20 - producing a homogeneous mixture of the active principle and the excipient, containing at least 50% of active principle;

- subjecting the homogeneous mixture to a high compression;

25 - grinding the compressed articles obtained; and

- putting into a form suitable for administration.